

Figure 1a

## Nucleic acid and amino acid sequence of TTX1 DRG sodium channel

```

tagcttgcttctgctaatactaccccaggccttttagacagagaacagatggcagatggag
1 -----+-----+-----+-----+-----+-----+-----+ 60
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tttcttattgccaatgcgcaaacgctgagccacctcatgatccccggaccccatgggttttc
61 -----+-----+-----+-----+-----+-----+-----+
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agtagacaacctgggctaagaagagatctccgaccttatagagcagcaagagtgtaaat
121 -----+-----+-----+-----+-----+-----+-----+
tcactctgttggacccgattcttctctagaggctggaatatctcgctgtttctcacattta

tcttccccaagaagaatgagaagATGGAGCTCCCCTTTGCGTCCGTGCGGAACCTACCAATT
181 -----+-----+-----+-----+-----+-----+-----+
agaaggggttcttcttactcttcTACCTCGAGGGGAAACGCAGGCACCCCTTGATGGTTAA

M E L P F A S V G T T N F -

TCAGACGGTTCACTCCAGAGTCACTGGCAGAGATCGAGAAGCAGATTGCTGCTCACCGCG
241 -----+-----+-----+-----+-----+-----+-----+
AGTCTGCCAAGTGAGGTCTCAGTGACCGTCTCTAGCTCTTCGTCTAACGACGAGTGGCGC

R R F T P E S L A E I E K Q I A A H R A -

CAGCCAAGAAGGCCAGAACCAAGCACAGAGGACAGGAGGACAAGGGCGAGAAGCCCAGGC
301 -----+-----+-----+-----+-----+-----+-----+
GTCCGGTTCTTCCGGTCTTGGTTCGTGTCTCCTGTCTCCTGTTCCCGCTCTTCCGGTCCG

A K K A R T K H R G Q E D K G E K P R P -

CTCAGCTGGACTTGAAAGACTGTAACCAGCTGCCCAAGTTCTATGGTGAGCTCCCAGCAG
361 -----+-----+-----+-----+-----+-----+-----+
GAGTCGACCTGAACCTTCTGACATTGGTTCGACGGGTTCAAGATACCACTCGAGGGTCGTC

Q L D L K D C N Q L P K F Y G E L P A E -

AACTGGTCGGGGAGCCCCCTGGAGGACCTAGACCCTTTCTACAGCACACACCGGACATTCA
421 -----+-----+-----+-----+-----+-----+-----+
TTGACCAGCCCCCTCGGGACCTCCTGGATCTGGGAAAGATGTCGTGTGTGGCCTGTAAGT

L V G E P L E D L D P F Y S T H R T F M -

TGGTGTGTAATAAAAGCAGGACCATTTCCAGATTTCAGTGCCACTTGGGCCCTGTGGCTCT
481 -----+-----+-----+-----+-----+-----+-----+
ACCACAACCTTATTTTCGTCTCGTAAAGGTCTAAGTCACGGTGAACCCGGGACACCGAGA

V L N K S R T I S R F S A T W A L W L F -

```

541 TCAGTCCCTTCAACCTGATCAGAAGAACAGCCATCAAAGTGTCTGTCCATTCTGCTTCT  
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 AGTCAGGGAAGTTGGACTAGTCTTCTTGTCTGGTAGTTTCACAGACAGGTAAGGACCAAGA  
 S P F N L I R R T A I K V S V H S W F S -

601 CCATATTCATCACCATCACTATTTTGGTCAACTGCGTGTGCATGACCCGAAGTATCTTC  
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 GGTATAAGTAGTGGTAGTGATAAAACCAGTTGACGCACACGTACTGGGCTTGACTAGAAG  
 I F I T I T I L V N C V C M T R T D L P -

661 CAGAGAAAGTCGAGTACGTCTTCACTGTCAATTACACCTTCGAGGCTCTGATTAAAGATAC  
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 E K V E Y V F T V I Y T F E A L I K I L -

721 TGGCAAGAGGGTTTGTCTAAATGAGTTCACTTATCTTCGAGATCCGTGGAAGTGGCTGG  
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 A R G F C L N E F T Y L R D P W N W L D -

781 ACTTCAGTGTCAATTACCTTGGCGTATGTGGGTGCAGCGATAGACCTCCGAGGAATCTCAG  
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 F S V I T L A Y V G A A I D L R G I S G -

841 GCCTGCGGACATTCCGAGTtctcagagccctgaaaactgtttctgtgatccaggactga  
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901 aggtcatcggtgggagccctgatccactcagtgaggaagctggccgacgtgactatcctca  
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 V F C L S V F A L V G L Q L F K G N L K -

1021 agaacaaatgcatcaggaacggaacagatccccacaaggctgacaacctctcatctgaaa  
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1081 tggcagaatacgtctccatcaagcctggtactacggatcccttactgtgcggaatgggt  
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1201 ttaactacaccagctttgattcctttgcgtgggcattcctctcactgttccgcctcatga  
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 4081 -----+-----+-----+-----+-----+-----+  
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4141 TCGACACCAGAAATAACCCATTTTCCAACGTGAATTCGACGATGGTGAATAACAAGTCCG  
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 4561 CCAAGAAACCCAGAAAGCCCATCCACGGCCCCCTGAATAAGTACCAAGGCTTCGTGTTTG  
 -----+-----+-----+-----+-----+-----+-----+  
 GGTTCCTTTGGGCTCTTCGGGTAGGGTGCCGGGGACTTATTCATGGTTCCGAAGCACAAAC  
 K K P Q K P I P R P L N K Y Q G F V F D -  
 4621 ACATCGTGACCAGGCAAGCCTTTGACATCATCATCATGGTTCTCATCTGCCTCAACATGA  
 -----+-----+-----+-----+-----+-----+-----+  
 TGTAGCACTGGTCCGTTCCGAAACTGTAGTAGTAGTACCAAGAGTAGACGGAGTTGTACT  
 I V T R Q A F D I I I M V L I C L N M I -  
 4681 TCACCATGATGGTGGAGACCGACGAGCAGGGCGAGGAGAAGACGAAGGTTCTGGGCAGAA  
 -----+-----+-----+-----+-----+-----+-----+  
 AGTGGTACTACCACCTCTGGCTGCTCGTCCCGCTCCTCTTCTGCTTCCAAGACCCGCTCT  
 T M M V E T D E Q G E E K T K V L G R I -



TCAACCAGTTCTTTGTGGCCGTCTTCACGGCCGAGTGTGTGATGAAGATGTTCCGCCCTGC  
 4741 -----+-----+-----+-----+-----+-----+-----+  
 AGTTGGTCAAGAAACACCGGCAGAAAGTGCCCGCTCACACACTACTTCTACAAGCGGGACG  
  
 N Q F F V A V F T G E C V M K M F A L R -  
  
 GACAGTACTACTTCACCAACGGCTGGAACGTGTTGACTTCATAGTGGTGTATCCTGTCCA  
 4801 -----+-----+-----+-----+-----+-----+-----+  
 CTGTCTATGATGAAGTGGTTGCCGACCTTGACACAAGCTGAAGTATCACCCTAGGACAGGT  
  
 Q Y Y F T N G W N V F D F I V V I L S I -  
  
 TTGGGAGTCTGCTGTTTTCTGCAATCCTTAAGTCACTGGAAAACACTTCTCCCCGACGC  
 4861 -----+-----+-----+-----+-----+-----+-----+  
 AACCCTCAGACGACAAAAGACGTTAGGAATTCAGTGACCTTTTGATGAAGAGGGGCTGCG  
  
 G S L L F S A I L K S L E N Y F S P T L -  
  
 TCTTCCGGGTCATCCGTCTGGCCAGGATCGGCCGCATCCTCAGGCTGATCCGAGCAGCCA  
 4921 -----+-----+-----+-----+-----+-----+-----+  
 AGAAGGCCAGTAGGCAGACCGGTCTAGCCGGCGTAGGAGTCCGACTAGGCTCGTCGGT  
  
 F R V I R L A R I G R I L R L I R A A K -  
  
 AGGGGATTCGCACGCTGCTCTTCGCCCTCATGATGTCCCTGCCCCGCCCTCTTCAACATCG  
 4981 -----+-----+-----+-----+-----+-----+-----+  
 TCCCTAAGCGTGCGACGAGAAGCGGGAGTACTACAGGCACGGCGGGGAGAAGTTGTAGC  
  
 G I R T L L F A L M M S L P A L F N I G -  
  
 GCCTCCTCCTCTTCCTCGTCATGTTTCATCTACTCCATCTTCGGCATGGCCAGCTTCGCTA  
 5041 -----+-----+-----+-----+-----+-----+-----+  
 CGGAGGAGGAGAAGGAGCAGTACAAGTAGATGAGGTAGAAGCCGTACCGGTGGAAGCGAT  
  
 L L L F L V M F I Y S I F G M A S F A N -  
  
 ACGTCGTGGACGAGGCCGGCATCGACGACATGTTCAACTTCAAGACCTTTGGCAACAGCA  
 5101 -----+-----+-----+-----+-----+-----+-----+  
 TGCAGCACCTGCTCCGGCCGTAGCTGCTGTACAAGTTGAAGTTCTGGAACCGTTGTCGT  
  
 V V D E A G I D D M F N F K T F G N S M -  
  
 TGCTGTGCCTGTTCCAGATCACCACCTCGGCCGGCTGGGACGGCCTCCTCAGCCCCATCC  
 5161 -----+-----+-----+-----+-----+-----+-----+  
 ACGACACGGACAAGGTCTAGTGGTGGAGCCGGCCGACCTGCCGGAGGAGTCCGGGGTAGG  
  
 L C L F Q I T T S A G W D G L L S P I L -  
  
 TCAACACGGGGCCTCCCTACTGCGACCCCAACCTGCCCAACAGCAACGGCTCCCGGGGGA  
 5221 -----+-----+-----+-----+-----+-----+-----+  
 AGTTGTGCCCCGGAGGGATGACGCTGGGGTTGGACGGGTGTCGTTGCCGAGGGCCCCCT  
  
 N T G P P Y C D P N L P N S N G S R G N -  
  
 ACTGCGGGAGCCCCGGCGGTGGGCATCATCTTCTTACCACCTACATCATCATCTCCTTCC  
 5281 -----+-----+-----+-----+-----+-----+-----+  
 TGACGCCCTCGGGCCGCCACCCGTAGTAGAAGAAGTGGTGGATGTAGTAGTAGAGGAAGG  
  
 C G S P A V G I I F F T T Y I I I S F L -

5341 TCATCGTGGTCAACATGTACATCGCAGTGAATTCTGGAGAACTTCAACCTAGCCACCGAGG  
 -----+-----+-----+-----+-----+-----+-----+  
 AGTAGCACCAGTTGTACATGTAGCGTCACTAAGACCTCTTGAAGTTGCATCGGTGGCTCC

I V V N M Y I A V I L E N F N V A T E E -  
 AGAGCACGGAGCCCCCTGAGCGAGGACGACTTCGACATGTTCTATGAGACCTGGGAGAAGT  
 5401 -----+-----+-----+-----+-----+-----+-----+  
 TCTCGTGCCTCGGGGACTCGCTCCTGCTGAAGCTGTACAAGATACTCTGGACCCTCTTCA

S T E P L S E D D F D M F Y E T W E K F -  
 TCGACCCGGAGGCCACCCAGTTCATTGCCTTTTCTGCCCTCTCAGACTTCGCGGACACGC  
 5461 -----+-----+-----+-----+-----+-----+-----+  
 AGCTGGGCCTCCGGTGGGTCAAGTAACGGAAAAGACGGGAGAGTCTGAAGCGCCTGTGCG

D P E A T Q F I A F S A L S D F A D T L -  
 TCTCCGGCCCTCTTAGAATCCCCAAACCCAACCAGAATATATTAATCCAGATGGACCTGC  
 5521 -----+-----+-----+-----+-----+-----+-----+  
 AGAGGCCGGGAGAATCTTAGGGGTTTGGGTTGGTCTTATATAATTAGGTCTACCTGGACG

S G P L R I P K P N Q N I L I Q M D L P -  
 CGTTGGTCCCCGGGGATAAGATCCACTGTCTGGACATCCTTTTTGCCTTCACAAAGAACG  
 5581 -----+-----+-----+-----+-----+-----+-----+  
 GCAACCAGGGGCCCTATTCTAGGTGACAGACCTGTAGGAAAAACGGAAGTGTCTTCTGC

L V P G D K I H C L D I L F A F T K N V -  
 TCTTGGGAGAATCCGGGGAGTTGGACTCCCTGAAGACCAATATGGAAGAGAAGTTTATGG  
 5641 -----+-----+-----+-----+-----+-----+-----+  
 AGAACCCTCTTAGGCCCTCAACCTGAGGGACTTCTGGTTATACCTTCTCTCAAATACC

L G E S G E L D S L K T N M E E K F M A -  
 CGACCAATCTCTCAAAGCATCCTATGAACCAATAGCCACCACCCTCCGGTGAAGCAGG  
 5701 -----+-----+-----+-----+-----+-----+-----+  
 GCTGGTTAGAGAGGTTTCGTAGGATACTTGGTTATCGGTGGTGGGAGGCCACCTTCGTCC

T N L S K A S Y E P I A T T L R W K Q E -  
 AAGACCTCTCAGCCACAGTCATTCAAAAGGCCTACCGGAGCTACATGCTGCACCGCTCCT  
 5761 -----+-----+-----+-----+-----+-----+-----+  
 TTCTCGAGAGTCGGTGTACAGTAAGTTTCCGATGGCCTCGATGTACGACGTGGCGAGGA

D L S A T V I Q K A Y R S Y M L H R S L -  
 TGACACTCTCCAACACCCTGCATGTGCCCAGGGCTGAGGAGGATGGCGTGTCACTTCCCG  
 5821 -----+-----+-----+-----+-----+-----+-----+  
 ACTGTGAGAGGTTGTGGGACGTACACGGCTCCCGACTCCTCCTACCGCACAGTGAAGGGC

T L S N T L H V P R A E E D G V S L P G -  
 GCGAAGGCTACATTACATTGATGGCAAACAGTGGACTCCCGGACAAATCAGAACTGCCT  
 5881 -----+-----+-----+-----+-----+-----+-----+  
 CCCTTCCGATGTAATGTAAGTACCGTTTGTACCTGAGGGCCTGTTTAGTCTTTGACGGA

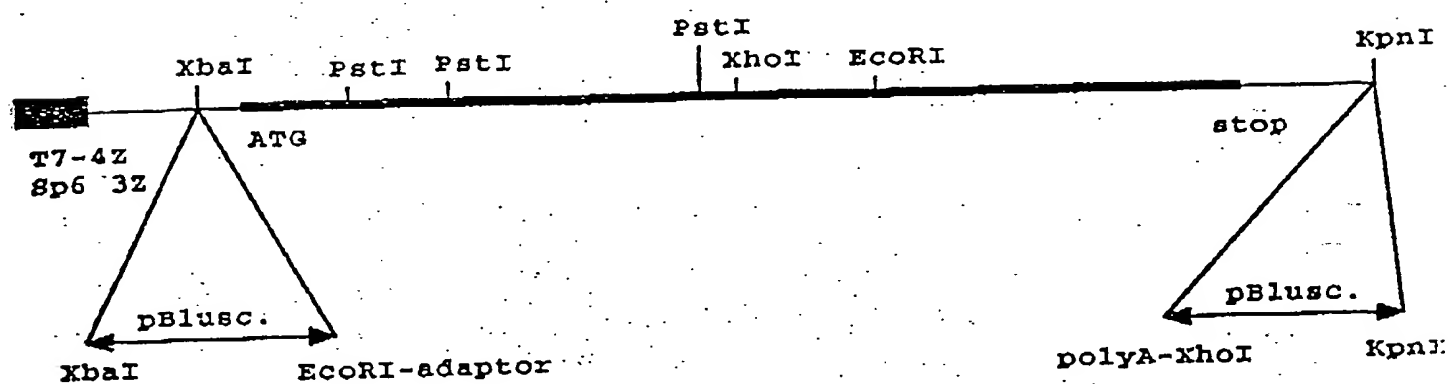
E G Y I T F M A N S G L P D K S E T A S -  
 CTGCTACGTCTTTCCCGCCATCCTATGACAGTGTACACAGGGGCCTGAGTGACCGGGCCA

5941 -----+-----+-----+-----+-----+-----+-----+  
GACGATGCAGAAAGGGCGGTAGGATACTGTCACAGTGGTCCCCGGACTCACTGGCCCCGGT  
A T S F P P S Y D S V T R G L S D R A N -  
ACATTAACCCATCTAGCTCAATGCAAAATGAAGATGAGGTGCTGCTAAGGAAGGAAACA  
6001 -----+-----+-----+-----+-----+-----+-----+  
TGTAATTGGGTAGATCGAGTTACGTTTTACTTCTACTCCAGCGACGATTCCCTTCCTTTGT  
I N P S S S M Q N E D E V A A K E G N S -  
GCCCTGGACCTCAGTGAAGGCACTCAGGCATGCACAGGGCAGGTTCCAATGTCTTTCTCT  
6061 -----+-----+-----+-----+-----+-----+-----+  
CGGGACCTGGAGTCACTTCCGTGAGTCCGTACGTGTCCCGTCCAAGGTTACAGAAAGAGA  
P G P Q \*  
GCTGTACTAACTCCTTCCCTCTGGAGGTGGCACCAACCTCCAGCCTCCACCAATGCATGT  
6121 -----+-----+-----+-----+-----+-----+-----+  
CGACATGATTGAGGAAGGGAGACCTCCACCGTGTTGAGGTGCGAGGTGGTTACGTACA  
CACTGGTCATGGTGTGAGAACTGAATGGGGACATCCTTGAGAAAGCCCCACCCCAATAG  
6181 -----+-----+-----+-----+-----+-----+-----+  
GTGACCAGTACCACAGTCTTGACTTACCCCTGTAGGAACTCTTTCGGGGGTGGGGTTATC  
GAATCAAAAGCCAAGGATACTCCTCCATTCTGACGTCCCTTCCGAGTTCCCAGAAGATGT  
6241 -----+-----+-----+-----+-----+-----+-----+  
CTTAGTTTTCGGTTCCTATGAGGAGGTAAGACTGCAGGGAAGGCTCAAGGGTCTTCTACA  
CATTGCTCCCTTCTGTTTGTGACCAGAGACGTGATTCACCAACTTCTCGGAGCCAGAGAC  
6301 -----+-----+-----+-----+-----+-----+-----+  
GTAACGAGGGAAGACAAACACTGGTCTCTGCACTAAGTGTTGAAGAGCCTCGGTCTCTG  
ACATAGCAAAGACTTTTCTGCTGGTGTGCGGCAGTCTTAGAGAAGTCACGTAGGGGTTGG  
6361 -----+-----+-----+-----+-----+-----+-----+  
TGTATCGTTTCTGAAAAGACGACCACAGCCCGTCAGAATCTCTTCAGTGCATCCCCAACC  
TACTGAGAATTAGGGTTTGCATGACTGCATGCTCACAGCTGCCGGACAATACCTGTGAGT  
6421 -----+-----+-----+-----+-----+-----+-----+  
ATGACTCTTAATCCCAAACGTACTGACGTACGAGTGTGACGGCCTGTTATGGACACTCA  
CGGCCATTAAAAATTAATATTTTTAAAGTTAAAAAAAAAAAAAAAAA  
6481 -----+-----+-----+-----+-----+-----+-----+ 6524  
GCCCGTAATTTAATTATAAAAAATTTCAATTTTTTTTTTTTTTTT

Figure 1b

Structure of SNS-B voltage-gated sodium channel in pGEM-3Z

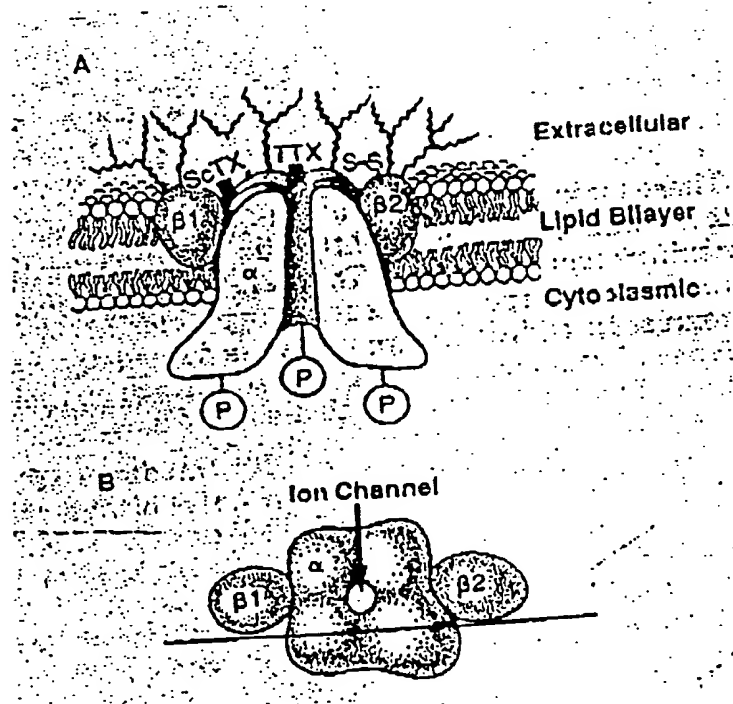
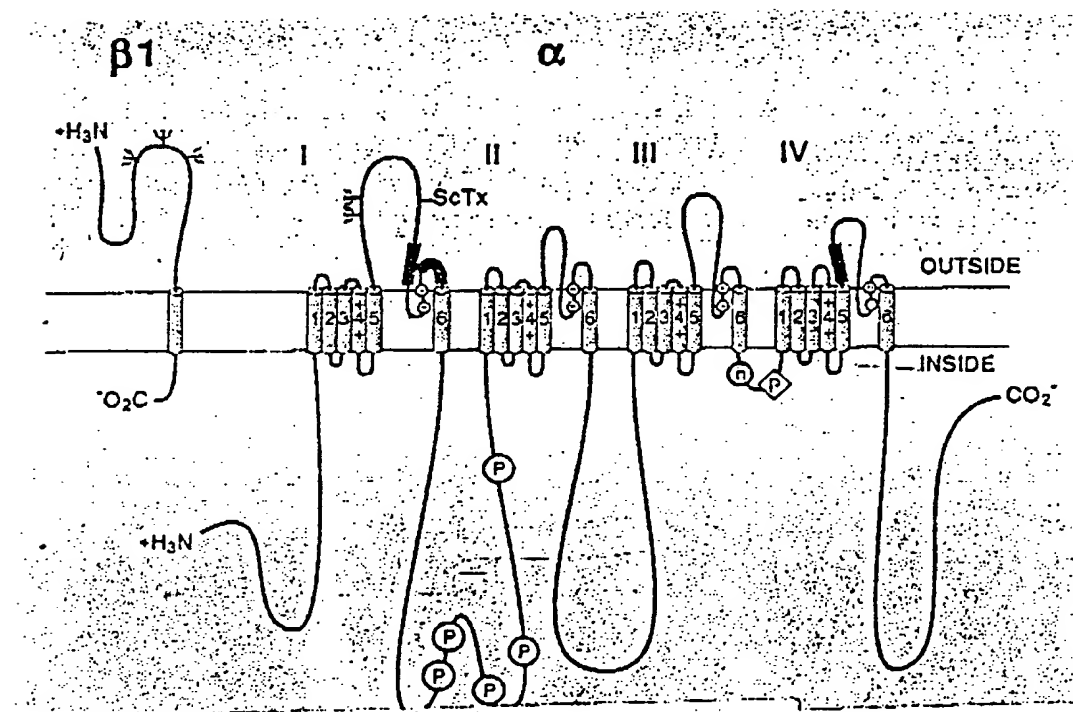
SNS-B voltage gated sodium channel  
PNC IB XOI- construct



Constructs were generated in pGem 3Z  
and pGem 4Z with bluescript polylinkers  
Linearization site is KPN1

Figure 1c

Schematised drawing of voltage-gated sodium channel (from Caterall 1992)

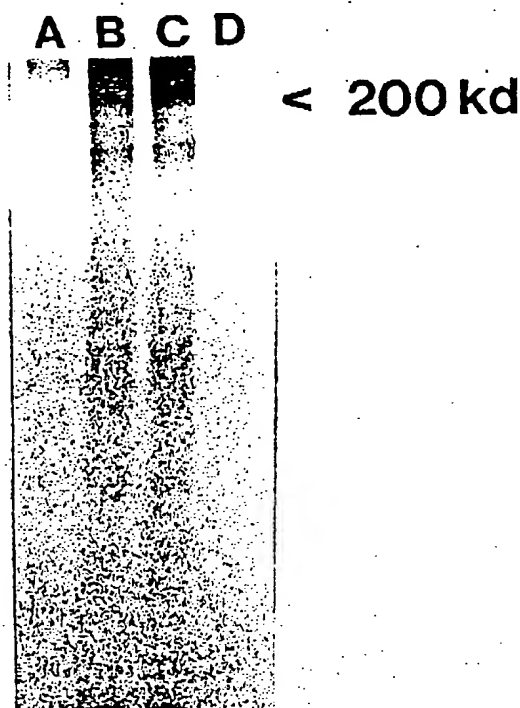


**FIGURE 2****Sequence of PCR primers for isolation of human clone probes**

- a) *Highly conserved regions of all sodium channels*
- 1) Position 2475-2510 S4 Domain II  
Degenerate primers (20-24mers) encoding amino acid residues  
RLLRVFKLAKSWPTL or non degenerate primers within this  
region e.g. 5' gcttgctgcgggtcttcaagc 3'
- 2) Position 3961 - 4010 S4 Domain III  
Degenerate primers encoding the complementary strand  
encoding residues LRALPLRALSRFEG or non degenerate  
primers within this region e.g. 5' atcgagacagagcccgagcg 3'
- b) *Unique sequence primers for SNS-homologues*  
e.g. residues with the region 2641-2680  
e.g. 5' acgggtgccgcaaggacggcgtctccgtgtggaacggcgagaag 3'  
and complementary sequence within the region 3375 and 3420  
e.g. 5' ggctatccttcctctccagctctcaccaggtatggagccaggt 3'

Figure 3

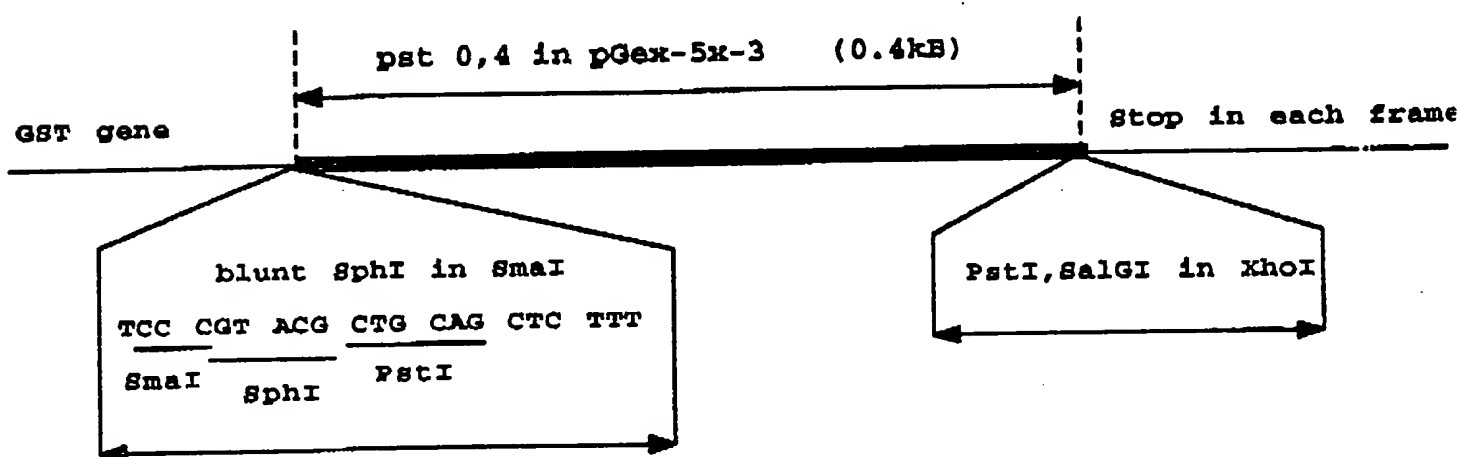
In vitro synthesis of S-35 methionine labelled SNS-B voltage gated sodium channel in a coupled transcription/translation system



Autoradiograph of a 7.5% SDS polyacrylamide gel, showing the migration of labelled proteins compared to the sizes of known molecular weight markers (Amersham rainbow markers). Lane A control, Lane B SNS-B, Lane C SNS-B, Lane D control. The predicted 200kDa band representing the SNS-B sodium channel is arrowed.

Figure 4a

# D1-extracellular construct for SNS antibody



# C-terminal (intracellular) construct for antibody

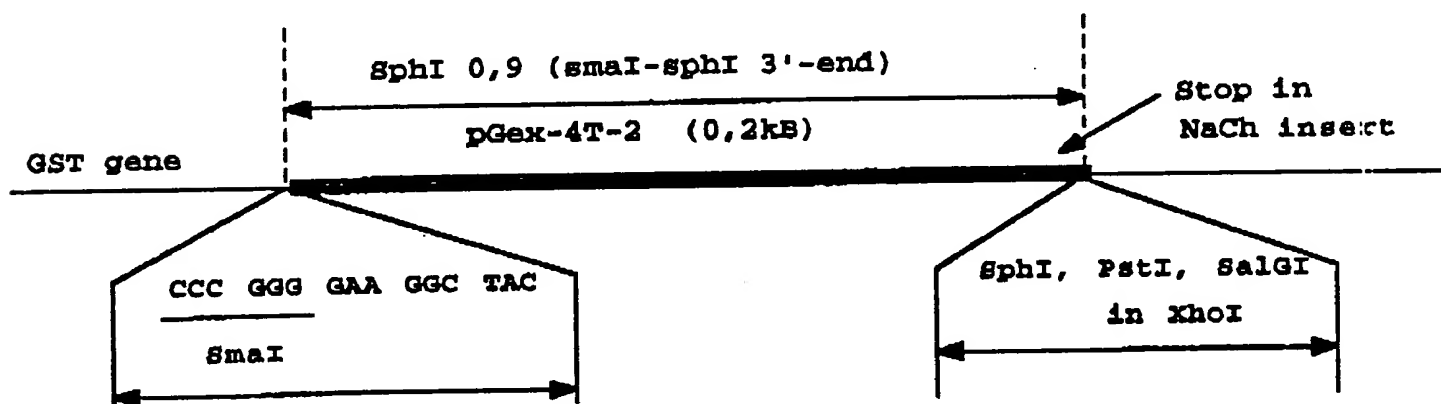
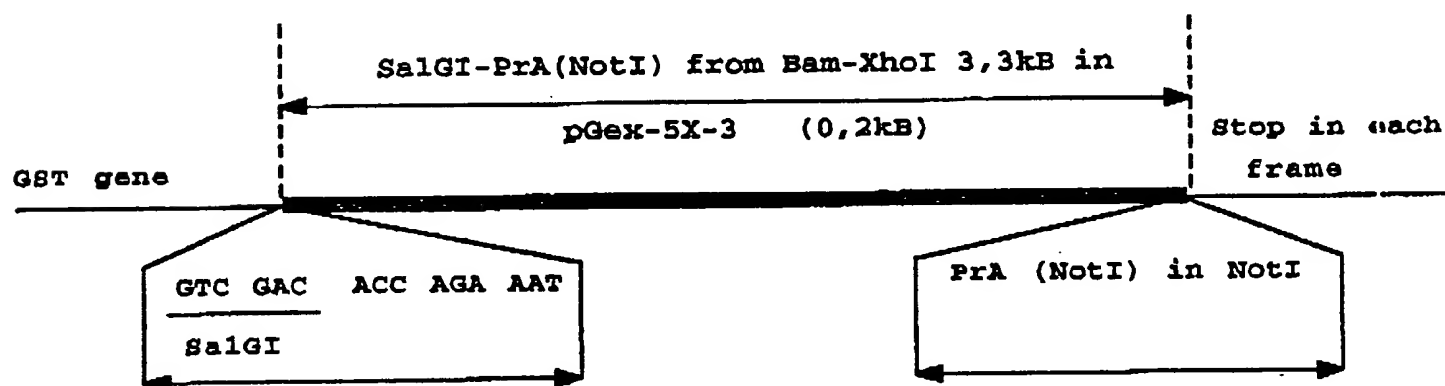




Figure 4b

## Extracellular D3 construct for antibody



## Intracellular D1-D2 construct for antibody

